Acute Kidney Injury in the era of the AKI e-alert: A National Survey

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Abstract

Background and objectives: Our aim was to use a national electronic AKI alert, to define the incidence and outcome of all episodes of community and hospital acquired adult AKI (AKI).

Design, setting, participants and measurements: A prospective national cohort study was undertaken in a population of 3.06 million. Data was collected between March 2015 and August 2015. All cases of adult (≥18yrs of age) AKI were identified to define the incidence and outcome of all episodes of community and hospital acquired AKI in adults. Mortality and renal outcomes were assessed at 90 days.

Results: There were a total of 31,601 alerts, representing 17,689 incident episodes giving an incidence of AKI of 577/100,000 population. Community acquired AKI accounted for 49.3% of all incident episodes, and 42% occurred in the context of pre-existing CKD (CKDEpi eGFR). 90-day mortality rate was 25.6%. 23.7% of episodes progressed to a higher AKI stage than the stage associated with the alert. AKI e-alert stage and peak AKI stage were associated

with mortality, and mortality was significantly higher for hospital acquired AKI compared to alerts generated in a community setting. Among patients who survived to 90 days following the AKI e-alert, those who were not hospitalized had a lower rate of renal recovery and a greater likelihood of developing an eGFR <60ml/min/1.73m^2 for the first time, which may be indicative of development of *de novo* CKD.

Conclusion: The reported incidence of AKI is far greater than previously reported incidence in studies reliant on clinical identification of adult AKI or hospital coding data. Although an e-alert system is IT driven and therefore lacks "intelligence" and clinical context, this data can be used to identify deficiencies in care, guide the development of appropriate intervention strategies and provide a baseline against which the effectiveness of these interventions may be measured.

Introduction

The reported incidence of AKI varies depending on its definition, the clinical setting in which it is detected, and the population studied. The definitions of AKI used in many previous studies in the literature varied, making direct comparison of these difficult. In 2009, the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) (1) report identified significant deficiencies in the management of AKI in hospitals in the U.K. This led to the development and implementation of strategies such as the use of electronic results reporting to aid early AKI recognition (2). In response the Royal College of Physicians, at a consensus conference in the UK, recommended the adoption of an e-alert system to aid in the early identification of AKI (3). Based on a presumption that early identification may help raise standards of care and improve patient outcomes, an automated real time e-alert system for AKI based on the Kidney Disease: Improving Global Outcomes (KDIGO) change in creatinine diagnostic criteria has been established and implemented nationally across all areas of the National Health Service in Wales. Using a centralised system of data collection the aim of this study was to provide a comprehensive characterisation of the ~~**base**~~ incidence and ~~**definition**~~ outcome of AKI identified by electronic alerts (AKI), ~~**and its outcome**~~ across both primary and secondary care.

Methods

Setting

The National Health Service in Wales which serves a population of 3.06 million is organised into seven Local Health Boards (Supplementary Figure 1). Data were collected in all health boards. The study was approved under Service Evaluation Project Registration.

Development of Electronic Reporting System

The all Wales Laboratory Information Management System (LIMS), (InterSystems TrakCare Lab) in real time automatically compares measured creatinine values on an individual patient against previous results, to generate alerts (Supplementary Figure 2), based on KDIGO AKI criteria (Supplementary Table 1). The definition of AKI therefore relies on creatinine but not urine output. A summary of the "rules" are shown in Supplementary Table 2 and each e-alert code together with the comment which accompanies the e-alert is shown in Supplementary Table 3. Any patient presenting with AKI but without a measurement of renal function in the previous 365 days will therefore not be included in the study.

Data Collection

Prospective data was collected for all cases of adult (≥18yrs of age) AKI in Wales between March 2015 and August 2015. Clinical location, patient age, AKI stage and the rule under which the AKI alert was generated was collected together with all measurements of renal function for up to 90 days following the AKI alert. An incident AKI episode was defined as 90 days i.e. any AKI e-alert for the same patient within 90 days the incident alert was not considered a new episode. Peak AKI stage was assigned by comparing the highest serum creatinine (SCr) value during an AKI incident episode with the baseline SCr of the incident alert. To prevent inclusion of known patients receiving renal replacement therapy, alerts transmitted by patients from a renal, renal transplant, or dialysis setting, and by patients who had a previous blood test in a dialysis setting were

excluded. All incident patients with AKI alerted for the first time in a non-renal location prior to transfer to the regional renal unit.
Incidence rate was calculated using Mid-2013 Office for National Statistics (ONS) Population Estimates. Patients for whom the first e-alert was generated from a creatinine value measured in primary care were classified as primary care AKI. All patients for which the first alert was issued during a hospital admission who also had a normal SCr value generated in a hospital setting within the preceding seven days were defined as Hospital acquired (HA)-AKI. Patients alerting in a non-inpatient setting (including Accident and Emergency/Acute assessment units) and not alerting in primary care were classified as non-primary care community acquired (CA)-AKI. Primary care and non-primary care CA-AKI therefore collectively represent CA-AKI.
Hospitalization of CA-AKI was defined as first or second measurement of renal function in an inpatient setting (within 7 days) following the alert. Mortality data were collected from the Welsh Demographic Service (WDS). Patients were censored at 1 year for survival analysis. Renal outcome analysis required patients to have 90 day follow up data available and included only those patients surviving at this time point. Linear regression analysis of renal outcome included surviving and non-surviving patients. Non-recovery from an AKI episode was defined as achievement of a serum creatinine (SCr) value closest to and within 90 days still consistent with the definition of AKI in comparisons to baseline SCr values. Pre-existing chronic kidney disease (PeCKD) was defined as an eGFR (calculated by CKDEpi eGFR formula (4)) <60ml/min/1.73m^2 derived from the baseline SCr. A worsening eGFR was calculated using the eGFR value closest to and within 90 days and was defined by a decline from baseline eGFR of >15% or >5ml/min/1.73m^2 (5).
The Welsh Index of Multiple deprivation is Welsh Government's official measure of relative deprivation. This generates a rank (WIMD score) for 1,909 lower super output geographical areas (LSOAs) in Wales based on eight domains; Income, Employment, Health, Education, Access to Services, Community Safety, Physical Environment, Housing (6). Patients were georeferenced to a LSOA of residence, and ranked according to WIMD score. Ranked data were categorised into percentiles, with percentile 1 the most deprived and percentile 100 the least deprived. Patients were aggregated to their geographic area (LSOA of residence), and incidence of AKI was calculated using the total adult population in each LSOA derived from Mid-2013 ONS Population Estimates.
Statistical analysis was carried out using SPSS software, version 20 (SPSS, Inc., Chicago, IL). Student's t test was used for analysis of normally distributed data. Categorical data were compared using a Pearson chi-squared test. Multivariate Cox proportional hazard modelling was used to analyze patient survival. P values less than 0.05 were considered statistically significant.

Validation

The diagnostic accuracy was determined by manually checking baseline creatinine value for a sample of 200 patients distributed across each "rule" and "e-alert Code", and across two Local Health Boards (LHBs). All the e-alerts generated conformed to the mathematical definition of AKI.
When known dialysis patients were not identified as such by the request through the "location code" a proportion of known dialysis patients generated an AKI e-

alert. This was only applicable to ABS1, ABS2 and DELTA1 codes (Supplementary Table 3). For ABS1 codes 89% of flagged patients were know dialysis patients. In total 105 patients were flagged by this code. These were all excluded from the analysis, and therefore 11% of the cohort identified by this code (12 patients) with probable AKI were excluded from the overall analysis. For ABS2 code, 26% of patients were dialysis patients. ABS2 accounted for a total of 562 patients. These have been included in the analysis and therefore by extrapolation 146 likely dialysis patients are included in the analysis. For the DELTA1 code 60% of those flagged and with a creatinine of >4.5mg/dL were dialysis patients. In total 89 patients were flagged by this code and had a creatinine of >4.5mg/dL. These were excluded, and therefore 40% of the cohort identified by this code (36 patients) with probable AKI were excluded. Using these criteria results in a false negative rate of 0.27% (exclusion of AKI patients) and a false positive rate of 0.83% (inclusion of known dialysis patients).

Results

Incidence and Demographics (Table 1)

We observed a total of 31,601 alerts. The majority (62.9%) of patients generated only one alert. Of those patients who triggered multiple e-alerts, 18.5% generated 2 alerts, 8.3% 3 alerts, 4.2% 4 alerts, 2.1% 5, 1.3% 6, with the remainder generating between 7-27 alerts. Only 2.8% of incident episodes were the result of a second episode from the same patient.

The alerts generated represent 17,689 episodes of AKI. This translates into an incidence of AKI of 577/100,000 population over the six-month time frame, and 1.2 cases per 100 person-years. The majority (78.7%) of episodes were classified as AKI1 at presentation, with 14.3% AKI2 and 7.0% AKI3. 23.7% of Stage 1 and Stage 2 episodes progressed to a higher peak AKI stage relative to the incident AKI alert stage. 15.1% (944) and 9.0% (562) of AKI stage 1 progressed to AKI stages 2 and 3 respectively, and, 21.8% (247) of AKI stage 2 progressed to AKI stage 3.

Community acquired and Hospital acquired AKI

The distribution of e-alerts by the location in which the alert was generated is shown in figure 1A. CA-AKI and HA-AKI accounted for 49.3% and 41.2% of all alerts respectively. The remaining 9.5% of alerts were generated in an inpatient setting but as no results were available for the previous 7 days it was not possible to confidently classify these as either CA- or HA-AKI. For both AKI in the community and acquired in hospital the overwhelming majority was AKI1.

The distribution of clinical locations for both non-primary care CA-AKI and HA-AKI alerts, stratified by AKI stage, is shown in figure 1B&C (and Supplementary Tables 4 & 5). The majority (53%) of AKI acquired in a non-primary care community setting is first detected, in the Accident and Emergency department. For Hospital acquired AKI, the largest single cohort is “acquired” in a General medical inpatient setting (25%), followed closely by the combination of general surgical and trauma/orthopaedics which accounts for 24% of all hospital acquired.

For community acquired incident AKI episodes, 30.6% were generated by an alert issued to primary care which represents 14.6% of all the incident AKI episodes. The remainder of CA-AKI was accounted for by patients alerting in a non-inpatient setting (including Accident and Emergency/Acute assessment

units) but excluding primary-care. Primary care AKI e-alerts were followed by hospital admission in 31% of cases (figure 2A). For primary care CA-AKI, admission was associated with greater severity of renal injury, with 26% of AKI1 admitted compared to 42% of AKI2 and 56% of AKI3. Non-primary care community AKI e-alerts were followed by hospital admission in 71% of cases (figure 2B). For this group admission to hospital was not related to AKI severity. There was a positive relationship between the time to repeat measurement of renal function and hospitalization with a significantly longer mean time for patients not hospitalised from both the primary care CA-AKI (7.4±13.8 vs. 11.9±14.1 days, p<0.0001) and non-primary care CA-AKI (2.7±7.6 vs. 11.1±16.2 days, p<0.0001). In non-hospitalised CA-AKI at the time of re-testing 18.2% had a further elevation of serum creatinine (compared to 40.9% of CA-AKI who were hospitalised). Of those CA-AKI not diagnosed in primary care, 19.9% of patients had a measurement of serum creatinine (that did not generate an e-alert) in the preceding 30 days.

Regional variations:

The geographical variation of AKI incidence is shown in Table 1. The low overall incidence in Powys and the higher incidence in Hywel Dda likely reflect the organisation of health care, with no secondary care services in Powys. Its population is served predominantly by hospital services in the neighbouring Hywel Dda health board (a smaller proportion may access hospital service in English hospitals for which we have no data). The high incidence in Cwm Taf occurs in both Hospital-acquired and Community-acquired groups. This board serves the most socially deprived population in the Principality. The relationship between incidence of AKI and patient socio-economic status is shown in Figure 3. There was a strong negative correlation between ranking by WIMD score and the incidence of AKI (r=-0.91, 95% CI -0.94 to -0.87 p<0.001).

Significance of an episode of AKI

Mortality: 90-day mortality for AKI is shown in figure 4. Overall 90-day mortality was 25.6%. Mortality was significantly higher (p<0.001) in HA-AKI compared to CA-AKI (Figure 4A). For CA-AKI mortality (Figure 4B&C) was significantly higher in the hospitalised cohort (p<0.001) and in non-primary care CA-AKI (p<0.001). Cox regression proportional hazard modelling analysis (with follow up data up to and including 12 months) demonstrated higher hazard of death associated with older age (HR 1.03, 95% CI, 1.029-1.034), more severe AKI at presentation (AKI 2/3 *versus* AKI; HR 1.43, 95% CI, 1.34-1.54), and peak AKI stage (AKI 2/3 *versus* AKI1; HR 2.36, 95% CI, 2.20-2.53). Increased hazard of death was associated with non-primary care CA-AKI (un-adjusted HR 1.77, 95% CI, 1.59-1.97; adjusted HR 1.65, 95% CI, 1.48-1.84, p<0.001) and HA-AKI (un-adjusted HR 2.04, 95% CI, 1.83-2.26: adjusted HR 1.98, 95% CI, 1.78-2.19; p<0.001) compared with primary care CA-AKI. For CA-AKI hospitalization was also associated with increased hazards of death (HR, 1.31; 95% CI, 1.23-1.39; p<0.001).

Renal Outcomes: The relationship between the incident AKI e-alert and subsequent renal function is shown in figure 5. Significantly more patients did not recover their renal function following an episode of HA-AKI compared with CA-AKI (14.6% vs. 7.9% p<0.001). In contrast more patients with CA-AKI and pre-existing CKD were likely to have worsening renal function following the AKI episode, than following HA-AKI (42.5% vs. 35.9%, p=0.002). For the whole

cohort, more severe AKI at presentation (AKI 2/3 *versus* AKI1; HR 1.82 95% CI, 1.64-2.03) and peak AKI stage (AKI 2/3 *versus* AKI1; HR 3.98, 95% CI, 3.49-4.54) were associated with non-recovery of renal function.

For CA-AKI picked up in primary care (Figure 5B), non-recovery of renal function was significantly higher than non-primary care CA-AKI ($p<0.001$). Similarly, AKI detected in primary care was associated with a greater likelihood of developing an eGFR <60ml/min/1.73m^2 for the first time ($p<0.001$), and of those patients with pre-existing CKD, patients with primary care CA-AKI were significantly more likely to experience a worsening eGFR ($p<0.001$). The relationship between admission to hospital and renal outcome for all community acquired AKI groups is shown in figure 5C. Hospitalization was associated with better outcome in terms of recovery from the acute episode ($p<0.001$), a lower proportion of patients developing an eGFR <60ml/min/1.73m^2 for the first time and less patients with pre-existing CKD experiencing worsening eGFR ($p<0.001$ for both parameters). By linear regression better acute outcome adjusted for both incident and peak AKI stage was also associated with hospitalization (HR 1.23; 95% CI 1.16-1.29; $p<0.001$).

Discussion

The majority of publications of large series characterising AKI rely on making and recording an accurate diagnosis of AKI through hospital coding or retrospective review of hospital records (7-10). Although providing essential information on the epidemiology of AKI there is significant potential for AKI episodes to be missed resulting in underestimation of true incidence of AKI. There are publications which have sought to overcome this via a biochemical identification of AKI as a trigger to identify the patients. These are however, either single centre hospital based studies (11, 12), or reliant on an electronic alert which was not based on an internationally agreed AKI definition (13). To address this, we used a national data set to provide a comprehensive characterisation of the incidence of electronic AKI alerts, and the subsequent clinical course.

The first key finding in this study is the high incidence of AKI. Previous studies have suggested an annual incidence of 200-300/100 000 in high income countries (14). The use of an alert based system for patient identification therefore overcomes systematic under-reporting of AKI associated with previous studies. The study also demonstrates a significant association of AKI with renal function at 90 days following the incident episode. For the whole cohort of over 17,000 patients, more than a quarter of the population either developed an eGFR <60ml/min/1.73m^2 for the first time – which may be indicative of the development of *de novo* CKD, or experienced worsening of pre-existing CKD after the incident AKI e-alert which may impact on the need to plan for long term provision of renal replacement therapy.

In contrast to studies describing HA-AKI, less is known regarding the characterisation of CA-AKI. Published studies in are in the main reliant on small patient numbers and due to geographical differences in disease patterns may not be directly applicable to all populations (15-17). The findings in this manuscript are however consistent with our previous publications (5, 18) and other recent smaller studies from Scotland (19) and Kentucky (20) demonstrating that CA-AKI represents a significant proportion of all AKI. The outcome for CA-AKI

defined by an eALERT is better than HA-AKI. This needs to be qualified by the observation a significant proportion of patients with CA-AKI are not admitted to hospital, and which therefore are not reported upon in the majority of publications which characterize the nature and outcome of CA-AKI.

In this study there is a significant mortality following an AKI e-alert. Mortality is clearly higher in the cohort of patients admitted to hospital, however it of note that even in CA-AKI patients who are not admitted to hospital there is a 90-day mortality of 10-15%, suggesting that even in this group for which admission may not be appropriate or desirable that AKI is a marker of frailty. In the surviving patients it is also of note that "non-admission" is associated with a significantly worse renal outcome. Whilst in some cases "non-admission" may be appropriate and reflect a conscious decision, e.g. in the setting of palliative care, our previous published data (5, 18) and the data on time to repeat measurement of renal function in this study suggest that "non-admission" is at least in part is due to lack of recognition of the significance of the alert. Our data is however consistent with the recent report of Sawheny in which non-admitted AKI whilst having a lower mortality was associated with greater non-recovery of renal function (21).

On a national level our data suggest regional variations in the incidence of AKI, with two areas in particular highlighted as outliers. The very small incidence in Powys likely reflects the rural nature of the area with the population relying on hospitals in neighbouring areas. Even accepting this discrepancy the reported incidence is very low. Access to hospital facilities, and renal services, has long been established as a factor influencing the reported incidence of CKD (22, 23), and it is interesting to speculate that the same may be true in terms of awareness of AKI. The second notable exception in AKI incidence is Cwm Taf. The Welsh Index of Multiple Deprivation (6), is produced at a small area level called Lower Super Output Area (LSOA), and is derived from a broad range of factors. 73 out of the 188 LSOAs in this LHB (39 per cent) are among the most deprived fifth in Wales. The tight association of AKI incidence and WIMD rank across the whole cohort supports the notion that a higher prevalence of AKI is associated with social deprivation as has been previously described for CKD (24, 25). Although beyond the scope of this study we speculate that this at least in part reflects a higher incidence of co-morbidities, which are AKI risk factors (26), in areas of social deprivation.

Although this study is to our knowledge the first national study using an e-alert based system to characterise the magnitude and impact of AKI, its findings need to be qualified by its limitations. As the e-alert system is IT driven it lacks "intelligence" and therefore there is no clinical context applied. For this reason the variation in serum creatinine seen in dialysis patients, unless specifically flagged by location, leads to a number of false positives. In order to minimise this impact we have excluded incident patients flagged by two codes (ABS1 and DELTA1) which will have also excluded some patients with true AKI. The study is also limited in that any patient presenting with AKI but without a measurement of renal function in the previous 365 days will not be included. Using an IT based approach also precludes inclusion of clinical information, such as patient co-morbidity and linkage to primary care data sets, and lacks the detail of the cause of AKI, the need for RRT, and does not shed light on the cause of death. It should also be noted that the data collected is for a six-month period and therefore potential seasonal effects on incidence may be lost. Although we

have collected data on the development of CKD this is limited by outcome data to 90 days only and therefore longer term studies of follow up are needed to truly describe the association with progressive CKD. It should also be noted that the outcomes reported in our study may be influenced by the transmission of the alert making direct comparison with other studies difficult. Despite these limitations our study provides the first large scale description of AKI, using a creatinine based electronic AKI alert.

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Disclosures; There are no competing interests

Table 1. Incidence/demography of AKI

Variable			
n/100,000 population (n)	577(17,689)		
AKI Severity, % (n)			
Stage 1	78.7(13,922)		
Stage 2	14.3 (2,522)		
Stage 3	7.0 (1,245)		
AKI Rule, % (n)			
Rule 1	9.9 (1,753)		
Rule 2	27.1 (4,799)		
Rule 3	63.0 (11,137)		
Clinical Location, % (n)			
Hospital	41.2 (7,288)		
Community	49.3 (8,724)		
	All AKI	HA-AKI	CA-AKI
Health Board, n/100,000 population (n)			
Abertawe Bro Morgannwg UHB	549 (2,857)	396.9	216.6
Aneurin Bevan UHB	550 (3,185)	189.9	265.9
Betsi Cadwaladr UHB	564 (3,906)	219.1	282.2

Cardiff and Vale UHB	513 (2,457)	247.7	239.1	
Cwm Taf UHB	814 (2,402)	313.8	429.0	
Hywel Dda UHB	693 (2,659)	258.4	392.5	
Powys THB	60 (80)	5.3	46.0	
	All AKI	AKI Stage 1	AKI Stage 2	AKI Stage 3
Mean age ±SD (yr)	71.1 ±17.0	71.0 ±17.3	71.8 ±15.9	70.5 ±15.9
Sex, % (n)				
Male	46.9 (8,285)	46.1 (6,407)	46.4 (1,171)	56.8 (707)
Female	53.1 (9,388)	53.9 (7,499)	53.6 (1,351)	43.2 (538)
Pre-existing CKD, % (n)	41.9 (6,877)	38.5 (5,354)	34.5 (870)	52.5 (653)
Mean baseline SCr (mg/dL)	1.0	1.0	0.9	1.4
Mean baseline eGFR (ml/min/1.73m^2)	71.6	72.0	74.4	61.7
Mean alert SCr (mg/dL)	1.8	1.5	2.1	4.7
Mean peak SCr (mg/dL)	2.3	1.9	2.5	5.3

Data on patient sex were missing for 16 cases and excluded from analysis of the sex variable. Baseline eGFR data were missing for 24 cases and excluded from analysis of the Pre-existing CKD variable. UHB, University Health Board; THB, Teaching Health Board; HA-AKI, Hospital acquired AKI; CA-AKI, Community acquired AKI; CKD, chronic kidney disease; SCr, Serum creatinine.

Figure Legends

Figure 1: Source of incident AKI e-alerts: [A] Distribution of AKI stages for hospital acquired AKI (HA-AKI) and community acquired AKI (CA-AKI). [B] Percentage and number of non-Primary Care CA-AKI patients, dividing according to clinical specialty and AKI stage. Clinical specialty data were missing for 289 cases and excluded from analysis. [C] Percentage and number of HA-AKI patients, dividing according to clinical specialty and AKI stage. Clinical specialty data were missing for 692 cases and excluded from analysis.

Figure 2: Hospitalization of community acquired AKI: [A] Percentage, average age, and, percentage with pre-existing CKD (shaded area of each bar), of primary care AKI (PC-AKI) patients that were hospitalised, dividing according to AKI stage (Total number of patients: Stage 1, 1,531; Stage 2, 255; Stage 3, 175). [B] Percentage, average age, and, percentage with pre-existing CKD (shaded area of each bar), of non-primary care AKI (non-PC-AKI) patients that were hospitalised, dividing according to AKI stage (Total number of patients: Stage 1, 3,727; Stage 2, 889; Stage 3, 542). PeCKD, pre-existing chronic kidney disease.

Figure 3: Relationship between incidence of AKI and the index of social deprivation. 221 cases with missing postcode data were excluded from analysis; 121 cases with English postcodes were excluded from analysis. WIMD, Welsh Index of Multiple deprivation where percentile is the most deprived and percentile 100 is the least deprived.

Figure 4: 90-day mortality associated with incident AKI e-alerts: [A] Percentage of AKI patients that died, dividing according to place of identification of AKI. [B] Percentage of CA-AKI patients that died, dividing according to hospitalization. [C] Percentage of CA-AKI patients that died, dividing according to place of identification of AKI. Mortality was significantly higher for all the "admitted groups" ($p<0.001$ compared to non-admitted groups). Mortality rates were comparable in the admitted non-primary care CA-AKI and HA-AKI groups, which were significantly higher than in the primary care AKI admitted cohort ($p=0.009$). Number of patients with data available indicated in parentheses in x axis. Shading indicates the proportion of patients that died by AKI Stage.

Figure 5: Renal outcome following AKI e-alerts: [A] Renal outcome of AKI patients, dividing according to place of identification of AKI. Of the patients for which 90-day follow up data were available, 1,841 (1,047, hospital acquired AKI (HA-AKI); 794, community acquired AKI (CA-AKI)) had died within the 90 day follow up period and were excluded from analysis. [B] Renal outcome of CA-AKI patients, dividing according to place of identification of AKI. Of the patients for which 90-day follow up data were available, 794 (121, Primary Care acquired AKI (PC-AKI); 673, non-primary care acquired AKI (non-PA-AKI)) had died within the 90 day follow up period and were excluded from analysis. 'Non-recovery' is expressed as a percentage of the whole cohort and was defined as a serum creatinine (SCr) value at 90 days following the AKI episode still in keeping with the definition of AKI in comparisons to baseline SCr values. 'No PeCKD and eGFR <60', and, 'PeCKD and worsening eGFR' are expressed as percentages of their respective PeCKD (pre-existing chronic kidney disease) cohorts. [C] Renal outcome of CA-AKI patients, dividing according to hospitalization. Of the patients for which 90-day follow up data were available, 794 (599, hospitalised community acquired AKI (Hosp. CA-AKI); 195, non-hospitalised community

acquired AKI (Non-hosp. CA-AKI)) had died within the 90 day follow up period and were excluded from analysis.

Supplementary Table 1. Staging of AKI

Stage	Serum creatinine
1	1.5 -1.9 times baseline or ≥26μmol/L increase
2	2.0-2.9 times baseline
3	3.0 times baseline or ≥354μmol/L

Supplementary Table 2. E-alert rules.

Rule	Description	Associated alert
1	>26μmol/L increase in creatinine in previous 48 hours	*Acute Kidney Injury alert: rising creatinine within last 48 hours*
2	>50% increase in creatinine in previous 7 days	*Acute Kidney Injury alert: rising creatinine within last 7 days*
3	>50% increase in creatinine against median result for previous 8-365 days	*Acute Kidney Injury alert – creatinine increase over baseline value*

Supplementary Table 3. AKI e-alert codes and their corresponding triggers, AKI rules, AKI stages

E-alert code	Trigger	AKI rule	AKI stage
DELTA1	D>26μmol/L and no other rule triggered	1	1
ABS1	C1/RV1>C1/RV2 and C1/RV1≥1.5 and C1>354μmol/L	2	3
ABS2	C1/RV2>C1/RV1 and C1/RV2≥1.5 and C1>354μmol/L	3	3
R1AKI1	C1/RV1>C1/RV2 and C1/RV1≥1.5 and C1/RV1<2.0	2	1
R1AKI2	C1/RV1>C1/RV2 and C1/RV1≥2.0 and C1/RV1<3.0	2	2
R1AKI3	C1/RV1>C1/RV2 and C1/RV1≥3.0	2	3
R2AKI1	C1/RV2>C1/RV1 and C1/RV2≥1.5 and	3	1

	C1/RV2<2.0		
R2AKI2	C1/RV2>C1/RV1 and C1/RV2≥2.0 and C1/RV2<3.0	3	2
R2AKI3	C1/RV2>C1/RV1 and C1/RV2≥3.0	3	3

D, Difference between C1 and lowest previous serum creatinine (SCr) value within 48 hours; C1, Index SCr value (current result entered and authorised on the LIMS); RV1, Reference value 1, lowest SCr value existing within previous 7 days; RV2, Reference value 2, median of SCr values existing within previous 8-365 days.

Supplementary Table 4. Specialties labelled 'Other' in Figure 1C

Specialty	N AKI episodes	%
Thoracic Medicine	85	1.45%
Medical Oncology	82	1.40%
Rheumatology	65	1.11%
Nephrology	54	0.92%
Endocrinology	45	0.77%
GP Other	30	0.51%
Cardiothoracic Surgery	29	0.50%
Rehabilitation	27	0.46%
Gynaecology	25	0.43%
Chemical Pathology	25	0.43%
Clinical Pharmacology and therapeutics	24	0.41%
Anaesthetics	17	0.29%
Palliative Medicine	15	0.26%
Pain Management	14	0.24%
Old Age Psychiatry	14	0.24%
Obstetrics (for patients using a bed)	13	0.22%
Dermatology	13	0.22%
Mental Illness	12	0.21%
ENT	10	0.17%
Paediatrics	9	0.15%
Ophthalmology	6	0.10%
Neurology	6	0.10%
Plastic Surgery	6	0.10%
Oral Surgery	5	0.09%
Not Known	5	0.09%
Obstetrics PN (outpatients)	4	0.07%
Haematology (non-clinical)	4	0.07%
Arts therapist	4	0.07%
Radiology	4	0.07%
Obstetrics AN (outpatients)	3	0.05%
Mental Handicap	2	0.03%
Community Medicine	2	0.03%
Genito Urinary Medicine	2	0.03%
Clinical Immunology and Allergy	2	0.03%
Midwifery	1	0.02%
General Pathology	1	0.02%
Restorative Dentistry	1	0.02%

Supplementary Table 5. Specialties labelled 'Other' in Fig 1D

Specialty	N of AKI episodes	%
Haematology (Clinical)	135	2.05%
Endocrinology	117	1.77%
Rehabilitation	95	1.44%
Obstetrics (for patients using a bed)	81	1.23%
Gynaecology	79	1.20%
Accident & Emergency	62	0.94%
Old Age Psychiatry	59	0.89%
Nephrology	59	0.89%
GP Other	50	0.76%
Clinical Oncology	47	0.71%
Neurosurgery	27	0.41%
Mental Illness	23	0.35%
Clinical Pharmacology and therapeutics	17	0.26%
ENT	16	0.24%
Paediatrics	15	0.23%
Medical Oncology	12	0.18%
Neurology	9	0.14%
Oral Surgery	7	0.11%
Plastic Surgery	7	0.11%
Community Medicine	6	0.09%
Rheumatology	4	0.06%
Dermatology	4	0.06%
Chemical Pathology	3	0.05%
Clinical Genetics	3	0.05%
Ophthalmology	2	0.03%
General Pathology	2	0.03%
Midwifery	2	0.03%
Restorative Dentistry	1	0.02%
Genito Urinary Medicine	1	0.02%
Psychotherapy	1	0.02%
Radiology	1	0.02%
Palliative Medicine	1	0.02%
Obstetrics AN (outpatients)	1	0.02%
Pain Management	1	0.02%
Mental Handicap	1	0.02%

Supplementary Figure Legends:

Supplementary Figure 1: Geographical location of Welsh Local Health boards and their associated descriptive demographic data. UHB, University Health Board; tHB, Teaching Health Board; DGH, District General Hospital; GP, General Practitioner.

Supplementary Figure 2: Algorithm for generating e-alerts for Acute Kidney Injury based on serum creatinine (SCr) changes with time. RV, Reference value, defined as the SCr value with which the index SCr value is compared; D, difference between current and lowest previous result within 48 hours; RI, Population reference interval.

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FIGURE 1

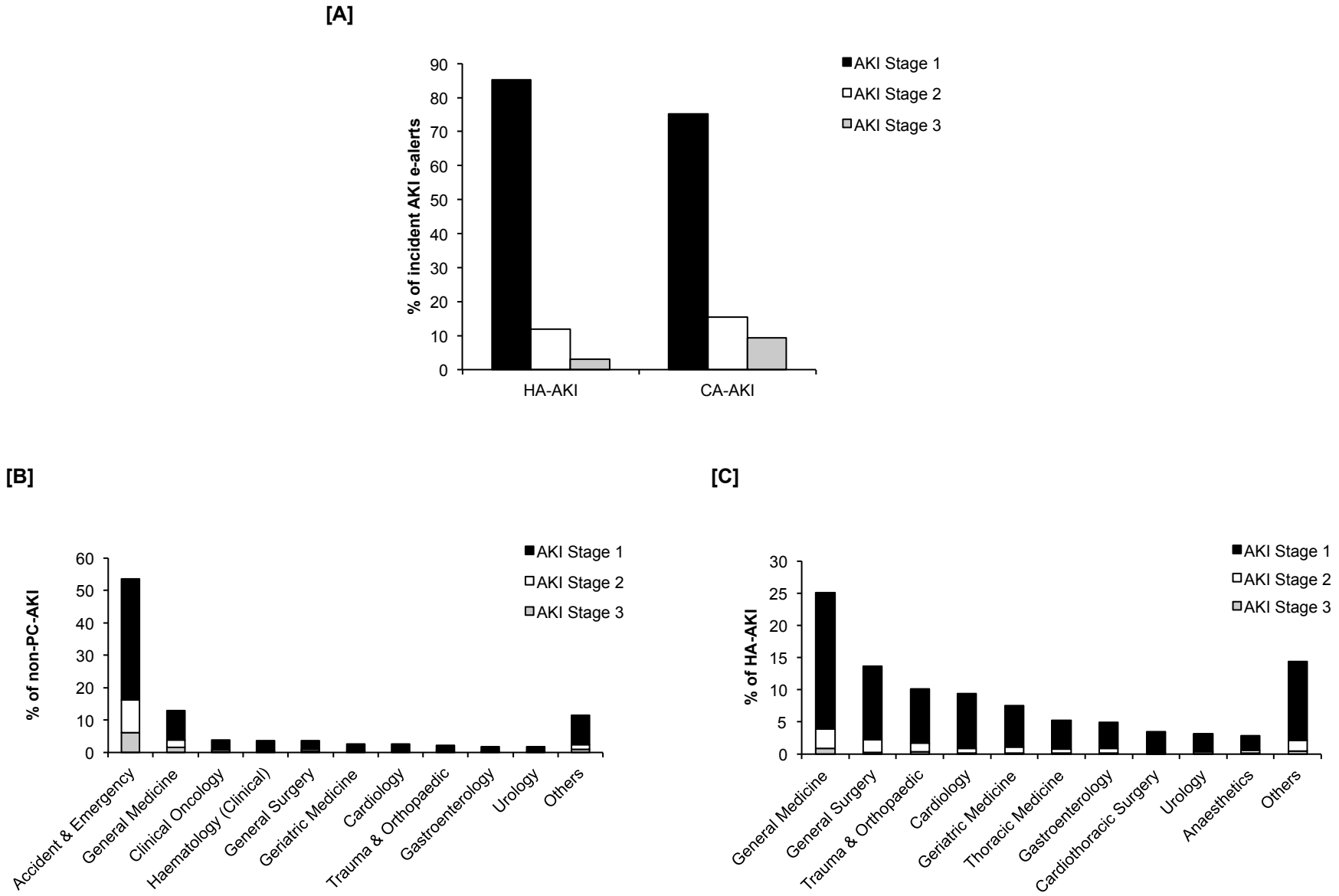
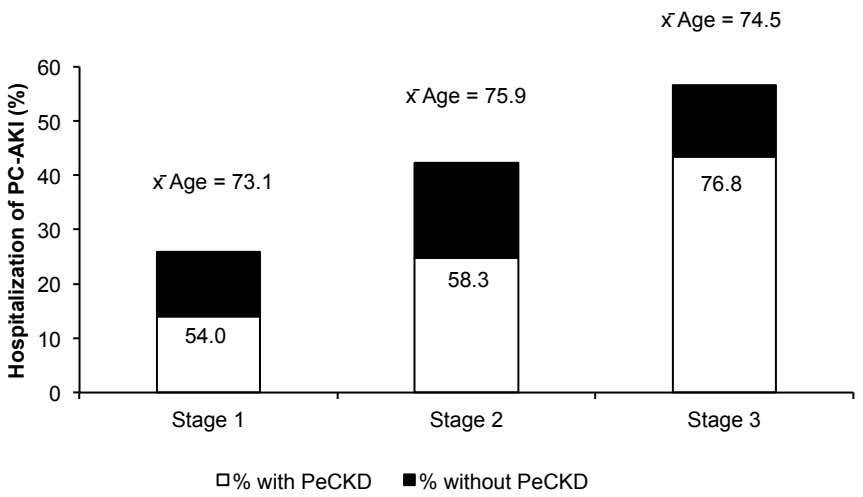

[A]
% of incident AKI e-alerts
90
80
70
60
50
40
30
20
10
0
HA-AKI
CA-AKI
AKI Stage 1
AKI Stage 2
AKI Stage 3
[B]
% of non-PC-AKI
60
50
40
30
20
10
0
Accident & Emergency
General Medicine
Clinical Oncology
Haematology (Clinical)
General Surgery
Geriatric Medicine
Cardiology
Trauma & Orthopaedic
Gastroenterology
Urology
Others
AKI Stage 1
AKI Stage 2
AKI Stage 3
[C]
% of HA-AKI
30
25
20
15
10
5
0
General Medicine
General Surgery
Trauma & Orthopaedic
Cardiology
Geriatric Medicine
Thoracic Medicine
Gastroenterology
Cardiothoracic Surgery
Urology
Anaesthetics
Others
AKI Stage 1
AKI Stage 2
AKI Stage 3

FIGURE 2

[A]


x̄ Age = 74.5
x̄ Age = 75.9
x̄ Age = 73.1
Hospitalization of PC-AKI (%)
60
50
40
30
20
10
0
76.8
58.3
54.0
Stage 1
Stage 2
Stage 3
% with PeCKD
% without PeCKD

[B]

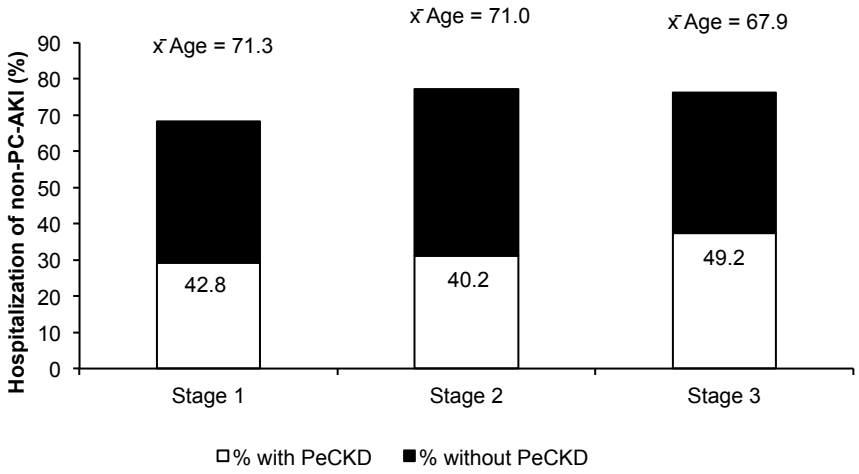

x̄ Age = 71.0
x̄ Age = 67.9
x̄ Age = 71.3
Hospitalization of non-PC-AKI (%)
90
80
70
60
50
40
30
20
10
0
49.2
42.8
40.2
Stage 1
Stage 2
Stage 3
% with PeCKD
% without PeCKD

FIGURE 3

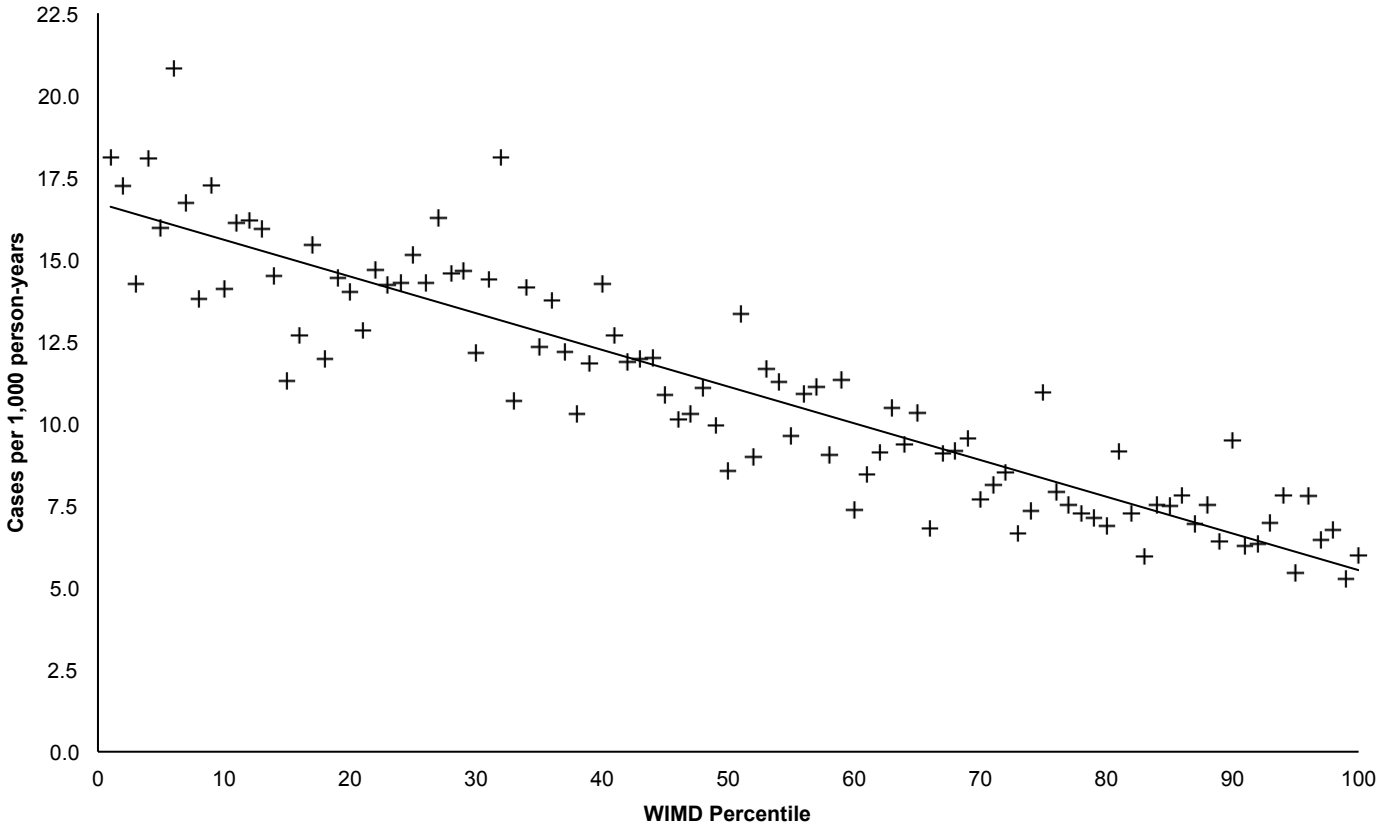

Cases per 1,000 person-years
22.5
20.0
17.5
15.0
12.5
10.0
7.5
5.0
2.5
0.0
0
10
20
30
40
50
60
70
80
90
100
WIMD Percentile

FIGURE 4

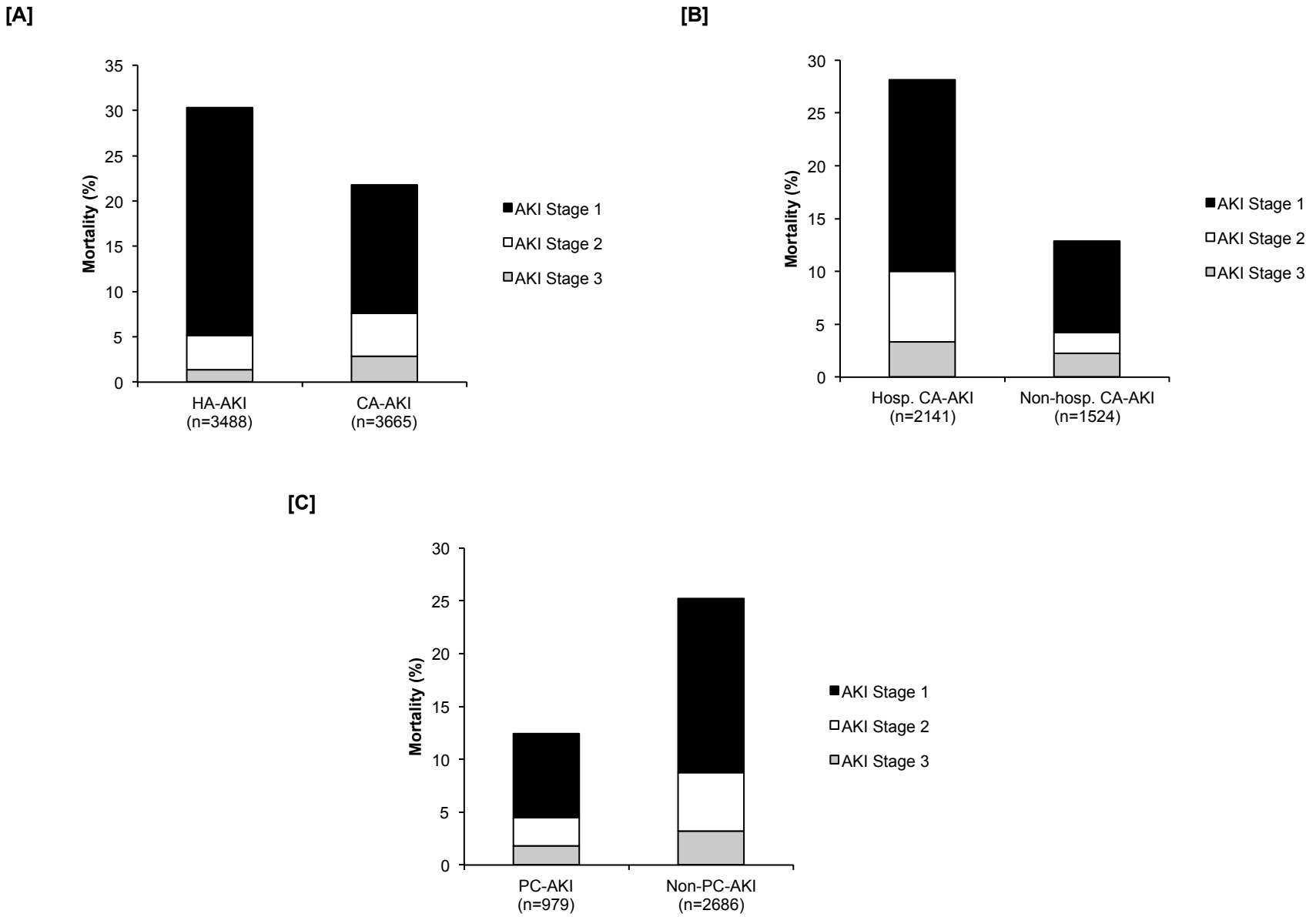
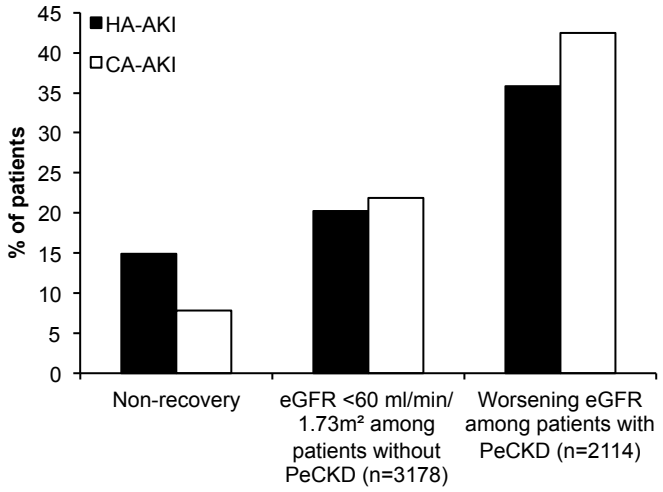
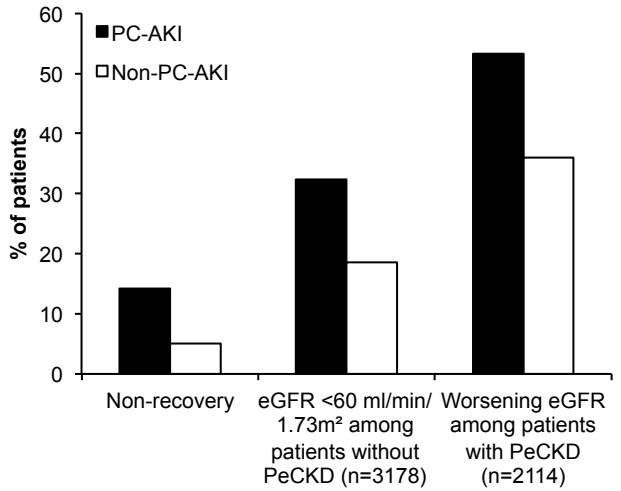

[A]
Mortality (%)
35
30
25
20
15
10
5
0
HA-AKI
(n=3488)
CA-AKI
(n=3665)
AKI Stage 1
AKI Stage 2
AKI Stage 3
[B]
Mortality (%)
30
25
20
15
10
5
0
Hosp. CA-AKI
(n=2141)
Non-hosp. CA-AKI
(n=1524)
AKI Stage 1
AKI Stage 2
AKI Stage 3
[C]
Mortality (%)
30
25
20
15
10
5
0
PC-AKI
(n=979)
Non-PC-AKI
(n=2686)
AKI Stage 1
AKI Stage 2
AKI Stage 3

FIGURE 5

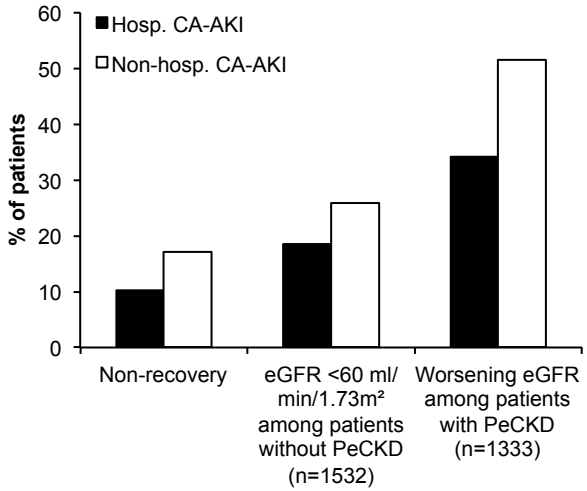
[A]


HA-AKI
CA-AKI
% of patients
45
40
35
30
25
20
15
10
5
0
Non-recovery
eGFR <60 ml/min/ 1.73m² among patients without PeCKD (n=3178)
Worsening eGFR among patients with PeCKD (n=2114)

[B]


PC-AKI
Non-PC-AKI
% of patients
60
50
40
30
20
10
0
Non-recovery
eGFR <60 ml/min/ 1.73m² among patients without PeCKD (n=3178)
Worsening eGFR among patients with PeCKD (n=2114)

[C]


Hosp. CA-AKI
Non-hosp. CA-AKI
% of patients
60
50
40
30
20
10
0
Non-recovery
eGFR <60 ml/ min/1.73m² among patients without PeCKD (n=1532)
Worsening eGFR among patients with PeCKD (n=1333)

SUPPLEMENTARY FIGURE 1